**Citation:**

Larsson SC, Giovannucci E, Wolk A. Dietary carbohydrate, glycemic index, and glycemic load in relation to risk of colorectal cancer in women. *Am J Epidemiol.* 2007 Feb 1;165(3):256-61. Epub 2006 Nov 21.

**PubMed ID:** 17118965

**Study Design:**

Prospective Cohort Study

**Class:**

B - Click here for explanation of classification scheme.

**Research Design and Implementation Rating:**

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

The purpose was to prospectively examine the associations between carbohydrate intake, glycemic index, and glycemic load and the risk of colorectal cancer in the Swedish Mammography Cohort Study.

**Inclusion Criteria:**

- Women in the Swedish Mammography Cohort (1987-1990)
- Women aged 40-76 years
- Central Swedish residence (Uppsala and Vastmanland counties)

**Exclusion Criteria:**

- Women outside the appropriate age range, women with an erroneous or msising national registration numbers, omitted dates on the questionnaire, questionable information about leaving the area, or information about date of death was lacking.
- Additionally, women were excluded if they had implausible energy intakes (3 standard deviations from the log transformed mean).
- Women were excluded if they were diagnosed with cancer (other than nonmelanoma skin cancer) prior to baseline.

**Description of Study Protocol:**

**Recruitment**

Women were participants in the Swedish Mammography Cohort, which was established between 1987 and 1990.

**Design** Prospective Cohort Study

**Blinding used (if applicable):** not applicable

**Intervention (if applicable):** not applicable

**Statistical Analysis**

- Participants were classified into quintiles of carbohydrate intake, glycemic index, and glycemic load.
- Cox proportional hazard models, stratified for age, were used to calculate the hazard ratios.
- In the multivariate models, the information was adjusted for education, body mass index, total energy intake and quartile of intakes of alcohol, fiber, folate, calcium, magnesium, and red meat.
- In a subanalyses: data from the second questionnaire was examined for physical activity, smoking, family history of colorectal cancer, aspirin use, postmenopausal hormones, and multivitamin supplements.

**Data Collection Summary:**

**Timing of Measurements**

- Baseline questionnaire about diet, education, weight and height in 1987-1990
- Second questionnaire in autumn of 1997
- 15.6 y follow-up

**Dependent Variables**

- Incidence of colorectal cancers ascertained by computerized record linkage of the study population with the national and regional Swedish Cancer registers

**Independent Variables**

- Carbohydrate intake
- Glycemic index and glycemic load were calculated
- Subjects completed a 67-item food frequency questionnaire at baseline and a 96-item food frequency questionnaire in 1997

**Control Variables**

- Education
- BMI
- Total energy intake
- Quartile of intakes of alcohol, fiber, folate, calcium, magnesium, and red meat

**Description of Actual Data Sample:**

**Initial N**: 66,651 women which was 74% of the source population. The final usable questionnaires were: 61,433 women in the first arm of this study.

**Attrition (final N):**

In 1997 a follow-up survey was mailed to 56,030 women who were still alive and residing in the area. 39,227 or 70% of the population returned their questionnaires. From this group, 36,616 questionnaires were analyzed and usable.

**Age:** 40-76 years

**Ethnicity:** Swedish population

**Other relevant demographics**

**Anthropometrics**

**Location:** Uppsala and Vastmanland counties

**Summary of Results:**

**Key Findings**

During follow-up through June 2005, 963,426 person-years of follow-up, 870 cases of colorectal cancer developed in this group of women.

Carbohydrate intake, glycemic index, and glycemic load had no significant association with colorectal cancer, colon cancer or rectal cancer, regardless of body mass index and alcohol consumption.

The multivariate hazard ratios for colorectal cancer comparing the highest with the lowest quintile were 1.10 (95% confidence interval: 0.85, 1.44) for carbohydrate intake, 1.00 (95% confidence interval: 0.75, 1.33) for glycemic index, and 1.06 (95% confidence interval: 0.81, 1.39) for glycemic load.

The associations of carbohydrate intake, glycemic index, and glycemic load with colorectal cancer did not differ across strata of physical activity or smoking status.

**Author Conclusion:**

In summary, although available evidence implicates hyperglycemia and hyperinsulinemia in colorectal cancer etiology, the results from this prospective study do not indicate an association between increasing glycemic load, which has been shown to predict postprandial blood glucose and insulin concentrations, and the risk of colorectal cancer in women. The authors also found no increase in colorectal cancer risk associated with a high carbohydrate intake or a high glycemic index. Future studies should examine the insulin index of foods in relation to cancer risk.

***Reviewer Comments:***

*Large sample size. Authors note the following limitations:*

- *Dietary intakes are measured with error*
- *Glycemic index values of some foods are currently based on results reported in only one or two studies with small sample sizes, leading to random variation in the estimated glycemic index values*

*Research Design and Implementation Criteria Checklist: Primary Research*

| Relevance Questions | | |
|---|---|---|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

| Validity Questions | | |
|---|---|---|
| **1.** | **Was the research question clearly stated?** | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| **2.** | **Was the selection of study subjects/patients free from bias?** | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | Yes |
| **3.** | **Were study groups comparable?** | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | N/A |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | N/A |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | N/A |

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| 3.4. | If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis? | Yes |
| 3.5. | If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.) | N/A |
| 3.6. | If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")? | N/A |
| **4.** | **Was method of handling withdrawals described?** | Yes |
| 4.1. | Were follow-up methods described and the same for all groups? | Yes |
| 4.2. | Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.) | Yes |
| 4.3. | Were all enrolled subjects/patients (in the original sample) accounted for? | Yes |
| 4.4. | Were reasons for withdrawals similar across groups? | Yes |
| 4.5. | If diagnostic test, was decision to perform reference test not dependent on results of test under study? | N/A |
| **5.** | **Was blinding used to prevent introduction of bias?** | Yes |
| 5.1. | In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate? | N/A |
| 5.2. | Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.) | Yes |
| 5.3. | In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded? | Yes |
| 5.4. | In case control study, was case definition explicit and case ascertainment not influenced by exposure status? | N/A |
| 5.5. | In diagnostic study, were test results blinded to patient history and other test results? | N/A |
| **6.** | **Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?** | Yes |
| 6.1. | In RCT or other intervention trial, were protocols described for all regimens studied? | N/A |
| 6.2. | In observational study, were interventions, study settings, and clinicians/provider described? | Yes |

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| 6.3. | Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect? | Yes |
| 6.4. | Was the amount of exposure and, if relevant, subject/patient compliance measured? | N/A |
| 6.5. | Were co-interventions (e.g., ancillary treatments, other therapies) described? | N/A |
| 6.6. | Were extra or unplanned treatments described? | N/A |
| 6.7. | Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups? | N/A |
| 6.8. | In diagnostic study, were details of test administration and replication sufficient? | N/A |
| **7.** | **Were outcomes clearly defined and the measurements valid and reliable?** | No |
| 7.1. | Were primary and secondary endpoints described and relevant to the question? | Yes |
| 7.2. | Were nutrition measures appropriate to question and outcomes of concern? | Yes |
| 7.3. | Was the period of follow-up long enough for important outcome(s) to occur? | Yes |
| 7.4. | Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures? | Yes |
| 7.5. | Was the measurement of effect at an appropriate level of precision? | No |
| 7.6. | Were other factors accounted for (measured) that could affect outcomes? | Yes |
| 7.7. | Were the measurements conducted consistently across groups? | N/A |
| **8.** | **Was the statistical analysis appropriate for the study design and type of outcome indicators?** | Yes |
| 8.1. | Were statistical analyses adequately described and the results reported appropriately? | Yes |
| 8.2. | Were correct statistical tests used and assumptions of test not violated? | Yes |
| 8.3. | Were statistics reported with levels of significance and/or confidence intervals? | Yes |
| 8.4. | Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)? | N/A |
| 8.5. | Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)? | Yes |
| 8.6. | Was clinical significance as well as statistical significance reported? | Yes |

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| 8.7. | If negative findings, was a power calculation reported to address type 2 error? | N/A |
| **9.** | **Are conclusions supported by results with biases and limitations taken into consideration?** | Yes |
| 9.1. | Is there a discussion of findings? | Yes |
| 9.2. | Are biases and study limitations identified and discussed? | Yes |
| **10.** | **Is bias due to study's funding or sponsorship unlikely?** | Yes |
| 10.1. | Were sources of funding and investigators' affiliations described? | Yes |
| 10.2. | Was the study free from apparent conflict of interest? | Yes |